inflammation and autoimmune disease. A novel series of orally available compounds that modulate the ATPase and exhibit therapeutic efficacy in murine disease models will be presented.

**13-Subg**
**New Avenues for Structure Determination of Membrane Proteins**
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Membrane proteins are of extreme relevance for all living cells. They are important for energy supply of the cells, transport across membranes, cell communication and play also vital roles in the pathogenesis of viruses and bacteria. Despite their important function, less than 300 membrane protein structures have been determined to date. One of the major limiting steps for the structure determination is the growth of well-ordered single crystals. New results of a rationale design of membrane protein crystallization are presented, that include screening for the reversibility of crystallization conditions, determination of phase diagrams, and determination of early events in nucleation and crystal growth by a combination of dynamic light scattering, SONICC, and tryptophan fluorescence microscopy. Nanocrystals detected, can either be used as seeds for growth of large single crystals or used for structure determination by femtosecond nanocrystallography. The latter method is based on a novel concept for structure determination, where X-ray diffraction ''snapshots'' are collected from a fully hydrated stream of nanocrystals, using femtosecond pulses from the world's first high energy X-ray free-electron laser, the Linac Coherent Light Source. The experiments show the proof of concept that diffraction of nanocrystals that contain only 100-10 000 membrane proteins can be observed and used for structure determination of large membrane protein complexes [1]. The femtosecond pulses are $10^{12}$ stronger than 3rd generation synchrotron sources and destroy any material that is placed in its focus, but as the femtosecond pulses are briefer than the time-scale of most damage processes, the method overcomes the problem of damage in crystallography. Femtosecond crystallography also opens new avenues for determination of molecular movies of protein dynamics.
Reference: [1] Chapman et al, 2011 Nature, 470, 73-77.

**14-Subg**
**Redox Coupled Conformational Changes in Cytochrome BC1 Complex: Implication to the Bifurcated Electron Transfer at the Quinol Oxidation Site**
**Di Xia, Ph.D.**[1], Lothar Esser[2], Wai-kwan Tang[2], Mingquan Zhang[3], Linda Yu[3], Chang-an Yu[3].
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The essential respiratory chain component cytochrome bc1 complex (ubiquinol cytochrome c oxido-reductase, bc1) couples the oxidation of ubiquinol to the vectorial proton movement across the membrane, contributing to the proton motive force essential for various cellular functions. In the bc1 complex, a high potential chain, consisting of the cyt c1 and ISP subunits, and a low potential chain, made up of hemes bL and bH, converge to the quinol oxidation or QP site. By inhibitor binding coupled crystallographic studies, the extrinsic domain of the iron-sulfur protein subunit (ISP-ED) was shown to undergo a binary inhibitor-type dependent conformation switch, leading to the ''surface affinity modulated ISP conformational switch'' hypothesis that provides a structural basis for the electron bifurcation at the QP site essential for the Q-cycle mechanism by which the bc1 complex operates. However, how this control of ISP-ED conformational switch is achieved under non-inhibitory conditions remains obscure. Here we show by redox coupled crystallographic analysis that the conformational switch of ISP-ED is correlated strongly with the redox potential of the high potential chain. Structural changes at the ISP-ED binding sites in response to redox changes were similar to those induced by binding to the QP site with different types of inhibitors. Functional implications will be discussed.

## Subgroup: Biopolymers in vivo

**15-Subg**
**Separating Excluded Volume and Chemical Effects of PEG on DNA Helix Formation**
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Small solutes affect protein and nucleic acid processes because of favorable or unfavorable chemical interactions of the solute with the biopolymer surface exposed or buried in the process. Large solutes also exclude volume and affect processes where biopolymer molecularity and/or shape changes. We recently developed an analysis to separate and interpret or predict excluded volume and chemical effects of a flexible coil polymer on a process. As a test system, of significance in its own right, we determined effects of the full series from ethylene glycol (EG) to polyethylene glycols (PEG) on the equilibrium constants for all-or-none intramolecular hairpin and intermolecular duplex formation by 12-nucleotide DNA strands. We find that helix-destabilizing chemical effects of PEG and its oligomers on these processes increase in proportion to the product of the amount of DNA surface exposed on melting and the amount of PEG surface that is accessible to this DNA; these chemical effects are completely described as the sum of interactions of PEG end and interior groups with this DNA surface. Helix-stabilizing excluded volume effects, once separated from these chemical effects, are quantitatively described by the analytical theory of Hermans, which predicts the excluded volume between a flexible polymer and a rigid molecule. An increase in PEG size at constant concentration of PEG monomer increases the excluded volume effect but decreases the chemical interaction effect, because in a large PEG coil a smaller fraction of the monomers are accessible to the DNA. Volume exclusion by PEG has a much larger effect on intermolecular duplex formation than on intramolecular hairpin formation.
Reference: PNAS 2011 108 (31) 12699-12704 (http://www.pnas.org/content/108/31/12699.long)
Supported by NIH grant GM47022 (TR) and a NIH Molecular Biophysics Traineeship to BK.

**16-Subg**
**Phase-Separating Aqueous Polymer Solutions as Simple Experimental Models for Cytoplasm**
**Christine Keating**.
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The interior of biological cells is crowded with macromolecules, heterogeneous in composition, and dynamic. We are developing simple experimental models for intracellular environments based on aqueous polymer solutions. Macromolecular crowding is modeled by inclusion of polymers such as polyethylene glycol or dextran; when both polymers are present aqueous phase separation can occur. Phase separation provides microcompartments corresponding to the dextran-rich and PEG-rich phase domains and enables control over the local concentration of not only the polymers themselves but also any molecules that accumulate in one of the phases by partitioning. Local enrichment of tenfold or greater can be maintained between the phases for solutes such as nucleic acids or proteins, and can be used to drive reactions that are concentration-dependent. Encapsulation of the aqueous two-phase systems within lipid vesicles having a semipermeable membrane provides a primitive model of biological cells capable of microcompartmentation, polarity, and asymmetric division. The synthesis and characterization of artificial cells and cell-like environments may provide new insight into how fundamental chemical and physical phenomena common to all cells may have shaped the development of early cells and underlie many of the seemingly complex behaviors of modern cells.

**17-Subg**
**RNA Folding in Crowded Solutions**
**Sarah A. Woodson**[1], Duncan Kilburn[2], Joon Ho Roh[3,4], R.M. Briber[3].
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Many non-coding RNAs fold into specific three-dimensional structures in order to act as catalysts or regulatory elements. Folded RNA structures are stabilized by K+ and Mg2+ ions that neutralize the phosphate negative charge and bind